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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/734,460	12/11/2000	Jerome B. Zeldis	9516-018	5112

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PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER
EVANS, CHARESSE L

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 11/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/734,460	ZELDIS, JEROME B.	
	Examiner	Art Unit	
	Charesse L. Evans	1615	

-- The MAILING DATE of this communication appears on th cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *3,6,19 and 32-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-10,12-18 and 20-23* is/are rejected.

7)☒ Claim(s) *11 and 24-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Action Summary

Acknowledgement is made of the receipt of the Response to Restriction Requirement wherein applicant, elected, with traverse, 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-amino-isoindoline. Applicant has reserved the right to prosecute the non-elected subject matter in one or more subsequent divisional or continuing application(s).

Claim 19 has not been considered as it does not read on applicant's species election which includes claims 1, 2, 4, 5, 7-18 and 20-31. Claim 19 should be included in the non-elected subject matter.

Claims 1, 2, 4, 5, 7-18 and 20-31 are active in this Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 5, 7-10, 12-18, 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muller et al (US 5,635,517). The claims are directed to a methods of preventing atheroschelerosis and stenosis in a mammal comprising administering an effective amount of a TNF-alpha inhibitor, such as 1-oxo-2-(2,6-dioxopiperidin-3yl)-4-aminoisoindoline.

Muller teaches a class of compounds used to decrease the levels of TNF-alpha. Specific compounds falling within the disclosed formula include 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline (column 7, lines 12). The referenced compounds are used to inhibit the undesirable effects of TNF-alpha and can be administered orally, rectally, or parenterally, alone or in combination with other therapeutic agents (column 4, lines 36-40). Oral dosage forms include tablets, capsules, dragees and similar shaped compressed pharmaceutical forms containing from 1 to 100mg of drug per unit dosage (column 6, lines 35-37). Please refer to Example 5 for an illustration of a preparation of tablets for chewing (column 9, Example 5). While the reference does not expressly teach applicant's claimed amounts, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the

prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). It is the position of the examiner that these are limitations that would be routinely determined by one of ordinary skill in the art, through minimal experimentation, as being suitable, absent the presentation of some unusual and/or unexpected results. Absent a clear showing of criticality, the determination of the particular ranges and administration regiment is within the skill of the ordinary worker as part of the process of normal optimization. The courts have held the "concentration limitations are obvious absent a showing of criticality." Azko v. E.E. Pont de Nemours, 1 USPQ 2d 1704 (Fed. Cir. 1987).

The cited reference does not expressly teach utilizing this compound for the prevention of atherosclerosis or restenosis. However, it does teach a method of reducing tumor necrosis factor-alpha (TNF-alpha) levels with this compound. Excessive or unregulated TNF-alpha production has been implicated in a number of disease states. Therefore, decreasing TNF-alpha levels constitutes a valuable therapeutic strategy for the treatment of these inflammatory, infectious, immunological or malignant diseases such as congestive heart failure (column 3, lines 59-65). Congestive heart failure is related to the group of ischemic heart diseases that also include atherosclerosis and coronary artery disease. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify

the reference of Muller by formulating a pharmaceutical regimen that would decrease or mitigate factors that are known to cause damage and impairment to the muscle fibers that relate to the contractility of the heart muscle.

Claim Objections

Claim 10 is objected to because of the following informalities: claim 10 refers to claims "...1, 2, 3" at the same time rather than only referring to only one claim at a time. Appropriate correction is required.

Claims 11 and 24-31 are objected to as being dependent upon a rejected base claim.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charesse L. Evans whose telephone number is 703-308-6400. The examiner can normally be reached on Monday - Thursday 7:00a - 4:30p; Alternating Fridays 7:00a - 3:30p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 703-308-2927. The fax phone

numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Charesse Evans
November 15, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600